RECEIVED
CENTRAL FAX CENTER
NOV 0 8 2006

Remarks

By the present communication, Claim 10 has been amended and Claims 33-39 have been added to define Applicant's invention with greater particularity. No new matter is introduced as the claimed subject matter is fully supported by the specification and claims as originally filed.

Specifically, new Claim 33 is based on original Claim 11 as amended in the Response to Final Rejection dated April 21, 2006, and additionally provides that a vector of the invention comprises a recombinant nucleic acid sequence encoding thiaminase I from *N. gruberi* as set forth in SEQ ID NO:3, support for which is found for example in Figure 6 of the specification as originally filed.

New Claims 34-35 are based on original Claim 8 and Claims 18-19 as amended in the Response to Final Rejection dated April 21, 2006, support which is found in the specification at for example page 40, lines 13-16, and page 11, lines 21-25.

New Claim 36, and Claims 37-39 dependent therefrom, are based on Claims 25-27 and 32 as amended in the Response to Final Rejection dated April 21, 2006, support for which is found in the specification at for example page 34, lines 25-29, and page 36, lines 12 and 21.

Upon entry of the present amendment, Claims 10 and 33-39 will be pending and under active prosecution. The Listing of Claims with appropriate status identifiers begins on page 2 of this communication

Claim Rejection under 35 U.S.C. § 112, first paragraph, enablement: Claim 10

The rejection of Claim 10 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement is respectfully traversed. However, in an effort to reduce the issues and expedite prosecution, Claim 10 as amended provides that the eukaryotic expression vector of the invention comprises a recombinant nucleic acid sequence encoding thiaminase I as set forth in SEQ ID NO:3. As stated by the Examiner (Office Action dated August 8, 2006, page 2, lines 11-12), the specification is enabling for a eukaryotic expression vector comprising a recombinant nucleic

RECEIVED
CENTRAL FAX CENTER
NOV 0 8 2006

acid sequence encoding thiaminase I of SEQ ID NO:3. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claim Rejection under 35 U.S.C. § 112, first paragraph, written description: Claim 10

The rejection of Claim 10 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement is respectfully traversed. As discussed above, Claim 10 as amended provides that the eukaryotic expression vector of the invention comprises a recombinant nucleic acid sequence encoding thiaminase I as set forth in SEQ ID NO:3. As stated by the Examiner (Office Action dated August 8, 2006, page 4, lines 23-25), the specification provides adequate written description for a eukaryotic expression vector comprising a recombinant nucleic acid sequence encoding thiaminase I of SEQ ID NO:3. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

New Claims

As discussed above, new Claim 33 is based on original Claim 11 as amended in the Response to Final Rejection dated April 21, 2006, and additionally provides that a vector of the invention comprises a recombinant nucleic acid sequence encoding thiaminase I from *N. gruberi* as set forth in SEQ ID NO:3. As asserted by the Examiner (Advisory Action dated May 9, 2006, Continuation of Item 11), Claim 33 (previous Claim 11) is enabled for SEQ ID NO:3:

> ... The prior rejection of claims 1, 3, 11, 25-27, and 32 is maintained for lack of enablement, for reasons of record. The claims are only enabled for SEQ ID NO:3, which encodes thiaminase I from N. gruberi, vectors containing said nucleic acids sequence, operably linked to a promoter, cells transformed in vitro by said vector, and specifically recited bacterium comprising said sequence... (emphasis added)

Thus, Applicants believe that Claim 33 is fully enabled as presented.

New Claims 34-35 are based on original Claim 8 and Claims 18-19 as amended in the Response to Final Rejection dated April 21, 2006. The Examiner's attention is drawn to the Final Office Action dated January 26, 2006, wherein Claims 18-19 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of written description. The Examiner had asserted (page

6, paragraph 2, lines 3-6) that the elements of the combination "both 90% identical to an equal length of at least 200 nucleotides" are not named together, and hence the combination allegedly lacked written description. However, the Examiner's attention is directed to the specification at page 40, lines 13-16, wherein the following statement is made regarding groupings of features contemplated by the claims:

> In addition, where features or aspect of the invention are described in terms of Markush groups or other grouping of alternatives, those skill in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

Accordingly, it is understood that Markush and other groupings of alternatives used in the specification contemplate each member of such groups individually.

Furthermore, express support for Claims 18-19 (now Claims 34-35) is found in the specification at page 11, lines 21-25:

> The invention also provides an isolated, purified, or enriched nucleic acid molecule that has a nucleotide sequence at least 90% identical, preferably at least 95%, 97%, 98%, 99%, or 100% to a portion of a *Naegleria gruberi* thiaminase gene or coding sequence at least 15, 17, 20, 25, 30, 35, 40, 50, 75, 100, 200, or even more nucleotides in length.

Accordingly, in view of the use of Markush and other groupings in the specification, as discussed on page 40, lines 13-16, each of the 6 percentages recited immediately above is specifically associated with each of the 12 nucleotide lengths recited immediately above. Thus, explicit support for the combination recited in Claim 18 (now Claim 34), i.e., 90% and 200 nucleotides, is found in the specification.

Accordingly, new Claim 34, and Claim 35 dependent therefrom, are fully supported by the specification and claims as originally filed.

New Claims 36-39, based on Claims 25-27 and 32 of the Response to Final Rejection dated April 21, 2006, are directed toward bacteria selected from the group consisting of avirulent *C. sporogenes*, avirulent *C. beijerinckii*, and attenuated, non-pathogenic *S. typhimurtumi*, which

bacteria comprise a recombinant nucleic acid sequence encoding thiaminase I from *N. gruberi* as set forth in SEQ ID NO:3. As stated in the Advisory Action dated May 9, 2006 (Continuation of Item 11), the rejection of previous Claims 25-27 and 32 was a new matter rejection, which was respectfully traversed, and for which the amendment was not entered:

> ... The prior rejection of claims 1, 3, 11, 25-27, and 32 under 112, 1st paragraph, for new matter, is maintained because the amendment is not entered, thus, the prior rejection is maintained with regard to the limitation of "non-pathogenic".

Specifically, Claims 25-27 and 32 of the Response to Final Rejection dated April 21, 2006 (now Claims 36-39) require avirulent *C. sporogenes*, support for which is found in the specification at, for example, page 36, line 21, avirulent *C. beijerinckii*, support for which is found in the specification at page 36, line 12, or attenuated non-pathogenic *S. typhimurium*, support for which is found in the specification at page 34, lines 25-29. Methods of rendering these bacteria avirulent or attenuated are found in the specification. For example, one of skill in the art would know that avirulent *C. sporogenes* is discussed by Kobayashi (*Vitamins* 1975, 49:45-51,) reference to which is provided in the specification at page 36, line 22. Furthermore, one of skill in the art would know that reference to Minton et al. 1995 (specification page 36, line 13) refers to Minton et al. (*FEMS Microbiol Rev.* 1995 Oct;17(3):357-64) which provides a description of the introduction of nitroreductase into a clostridial expression vector and introduction of the resultant plasmid into *C. beijerinckii*. Finally, one of skill in the art would know that discussion and methods of production of attenuated non-pathogenic S. *typhimurium* for cancer therapy is found in Low *et al.*, 1999 (*Nature Biotech.* 17:37-41,) Pawelek *et al.*, (*Cancer Res.* 57:4537-4544) or Salzman *et al.*, 1997 (*J. Pediatr. Surg.* 32:301-306.)

Accordingly, Claims 36-39 introduce no new matter and are fully supported by the specification and claims as originally filed.

Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. In the event that any matters remain to be resolved in view of this communication, the Examiner is

encouraged to call the undersigned so that a prompt disposition of this application can be achieved. The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date: November 8, 2006

By _____

FOLEY & LARDNER LLP
Customer Number: 30542
Telephone: (858) 847-6767
Facsimile: (858) 792-6773

Richard J. Warburg
Registration No. 32,327
Attorney for Applicant